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RESEARCH ARTICLE

RECENT UNDERSTANDING OF ECTODERMAL DYSPLASIA

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Abstract

The Ectodermal dysplasia (ED) is a rare hereditary disorder involving absence or deficiency of structures derived from ectoderm. Ectodermal dysplasia is caused by the mutation or deletion of certain genes located on different chromosomes. More than 200 EDs have been described. Signs of ED comprising abnormal hair (Atrichosis/Hypotrichosis), abnormal or missing teeth (Anodontia/ Hypodontia - peg or conical shaped), abnormal nail (Onychodysplasia) and decreased or absent sweating due to a lack of sweat glands (Dyshidrosis or Hypohidrosis/ Anhidrosis). Such abnormal appearance may affect normal social and psychological development in young patients. ED can be classified into two groups i.e. Hypohidrotic ED and Hidrotic ED. Hypohidrotic ED is most prevalent. The objective of this article is to review the diagnosis and management of Ectodermal dysplasia. Areas discussed include the prevalence of disease, presentation, diagnosis, and contemporary treatment. There is also a great need for improved therapies to combat this frustrating illness.

Introduction:-

The Ectodermal dysplasia (ED) is a rare hereditary disorder involving absence or deficiency of structures derived from ectoderm. Ectoderm is one of the germ layer formed during embryogenesis. The ectoderm develops into the surface ectoderm, neural crest, and the neural tube. The surface ectoderm develops into epidermis, hair, nails, sweat glands, sebaceous glands, mammary glands, tooth enamel, cornea, lens of the eye, retina and the epithelium of the mouth and nose. Cutaneous structures or appendages are developed through complex reciprocal signaling interactions between the ectoderm and the underlying mesoderm[1-3]. Dysplasia means abnormal development or growth of tissues, organs, or cells. All Ectodermal dysplasias are present from birth and are non-progressive.[4] Worldwide around 7,000 people have been diagnosed with an Ectodermal dysplasia condition.[5] The database of the National Foundation for Ectodermal Dysplasias (NFED) – the North American support group for ED – has registered more than 5,200 individuals with ED from 50 states in the US, and from over 70 countries. More than 1,900 (36.5%) of them have hypohidrotic type of ED, and more than 2,600 (50%) have no specific clinical diagnosis.[6] Tanner states in the case of Ectodermal dysplasia that such abnormal appearance may affect normal social and psychological development in young patients.[7]

Feire-Maia (1971) was the first to propose that a definition of EDs be based on four signs: Trichodysplasia (hair), dental defects (teeth), Onychodysplasia (nails), and Dyshidrosis (sweat glands). In the Feire-Maia definition, Group A – a pure ED – comprised disorders with signs affecting at least two of these structures, and Group B – an ED syndrome – comprised disorders involving one of these four structures and another ectodermal malformation.[8] Besides the classical ectodermal signs, other structures derived from the embryonic ectoderm may be affected, among them the mammary gland, thyroid gland, thymus, cornea, conjunctiva, lacrimal gland, lacrimal duct[9], and Meibomian gland[10]. Signs and symptoms of otolaryngologic manifestations in ED are well-known clinically but few

cases only reported in the literature. One case report of a patient with hypohidrotic ED who presented dysphagia and pneumonia postulated that laryngeal incompetence was related to recurrent chest infections.[11]

Etiology and Classification:-
Ectodermal dysplasia is presented with different types is caused by the mutation or deletion of certain genes located on different chromosomes. It displays an autosomal dominant, autosomal recessive or X-linked pattern of inheritance.[12,13] More than 200 EDs have been described[14,15].

ED can be classified into two groups - Hypohidrotic ED (sweat glands are absent or decreased); and Hidrotic ED (sweat glands are normal).

Subgroups:- [16,17,18]
According to the presence or absence of the four primary ectodermal dysplasia (ED) defects,
Different subgroups are created:
1. ED1: Trichodysplasia (hair dysplasia)
2. ED2: Hypodontia/ Anodontia (dental dysplasia)
3. ED3: Onychodysplasia (nail dysplasia)
4. ED4: Dyshidrosis (sweat gland dysplasia).

Based on the above, the 150 different types of Ectodermal dysplasias are categorized into one of the following subgroups made up from the primary ED defects: as Subgroup 1-2-3-4, 1-2-3, 1-2-4,1-2,1-3, 1-4, 2-3-4, 2-3, 2-4, 3,4. Hypohidrotic ED which falls under subgroup 1-2-3-4 and Hydrotic ED which comes under subgroup 1-2-3. Ectrodactyly-ED-clefting syndrome, Rapp-Hodgkin hypohidrotic ED, Ankyloblepharon, ectodermal defects, cleft lip/palate (AEC) or Hay-Wells syndrome are the three most recognized ectodermal dysplasia syndromes fall into the subgroup 1-2-3-4, as they show features from all four of the primary ED defects.

Discussion:-
Hypohidrotic ED is the most common of the EDs [6,8,14,15,19] and can have varying modes of inheritance – x-linked (OMIM 305100), autosomal dominant (OMIM 129490), or autosomal recessive (OMIM 224900) – all with a similar phenotype.

Hypohidrotic and Hidrotic ectodermal dysplasia (HED):-
Hypohidrotic ectodermal dysplasia (HED) also known as Anhidrotic ectodermal dysplasia and Christ- Siemens-Touraine syndrome. HED is characterized by a triad of signs comprising sparse hair (Atrichosis/Hypotrichosis), abnormal (peg or conical shaped) or missing teeth (Anodontia/ Hypodontia), and decreased or absent sweating due to a lack of sweat glands (Anhidrosis/ Hypohidrosis) which leads to heat intolerance and may cause recurrent, potentially life-threatening hyperthermic episodes. The nails are usually normal. X-linked hypohidrotic ED was first described by Thurnam in1848 and a few decades later, Darwin in 1875 described a kindred of men from Scinde who had the condition.[9,20] Scaling skin and a collodion membrane in the neonatal period have been reported in a few children with hypohidrotic ED, and may be an early indication of the diagnosis.[21,22,23] Kere et al. (1996) showed that a mutation in a gene in the Xq12–Xq13.1region, which encodes for a tran-smembrane protein called ectodysplasin, causes x-linked hypohidrotic ED.[17] Monreal et al. later identified the gene in which this mutation occurred and named the gene EDA.[24] Characteristic facial features of frontal bossing, saddle nose, maxillary hypoplasia, and hyperkeratotic wrinkles around the eyes give them a similar facial appearance.[19,25] Hidrotic Ectodermal Dysplasia (Clouston Syndrome) is characterized by nail dystrophy, alopecia, and hyperkeratosis in palmoplantar region.

Other EDs:- [18,26,27,28]
Ectrodactyly-ectodermal defects (EEC) syndrome (also known as "Split hand–split foot ectodermal dysplasia– cleft syndrome") is characterized by ectrodactyly, ectodermal dysplasia, and orofacial clefts (cleft lip/palate). Rapp-Hodgkin Ectodermal Dysplasia or Rapp-Hodgkin syndrome (RHS) is characterized by the association of Anhidrotic ectodermal dysplasia with cleft lip/palate.

Signs and symptoms of ED:-
Facial features:-

Facial asymmetry, frontal bossing, depressed nasal bridge (saddle nose), reduced vertical facial height and depth, small palatal and cranial base widths, high-set orbits, thick lips, large chin/Hypoplasia of the mandible. Senile appearance of the face present in this cases.

Eyes: Dry eye, chronic conjunctivitis, blepharitis, some cases keratoconus noticed.

Oral cavity and teeth:-
An hypohidrotic ectodermal dysplasia presents the most dental anomalies. That include 80% are hypodontia or oligodontia (reduced number of teeth) and remaining are anodontia (absence of teeth). Kohachiro Ohno et.al compiled in his article, there were 17 cases of anodontia associated with ectodermal dysplasia are have been reported during last 50 years. In these cases most cases were not true anodontia, but nearly anodontia or oligodontia.[29] Other dental defects are polydontia, dysplastic teeth, retained primary teeth, deficient enamel development (amelogenesis imperfecta), dentine deficiency (dentinogenesis imperfecta), and underdevelopment of the alveolar ridge.[30] Teeth are in peg shaped or conical shaped, abnormal enamel present. Reduced salivary secretion, dry oral mucosa and hoarse voice also noticed.

Skin:-
The skin is dry, thin, smooth (hypohidrosis), hypopigmentation (lack of pigmentation), with patches of hyperkeratosis and or eczematous. Palmoplantar hyperkeratosis may also present. Some cases skin atrophy also present.

Typical skin symptoms are inflammatory vesicles, which later develop into characteristic hyper pigmented striae.[31] The hair on scalp and body are generally blond and scanty. Hair appears as thin, sparse (Trichodysplasia/ hypotrichosis), coarse, brittle, curly. Body hair follicles are usually scanty or absent.

Nails:-
Nails may be thick, ridged, hyper convex and discoloured with striation, slow growing, or easily brittle. Few cases micronychia, onycholysis can be noticed.

Glands:-
The oral and nasal mucous glands, the salivary glands and the mammary glands may be hypoplastic or absent. The mucous glands may be absent in the whole gastrointestinal (GI) tract and respiratory tree. Eccrine sweat glands may be absent or sparse so that over heat is common. Recurrent high fever also experienced.

Other features:-
In some cases, decreased function of certain components of the immune system (e.g., depressed lymphocyte function, cellular immune hypofunction), potentially causing an increased susceptibility to certain infections and/or allergic conditions. Many affected infants and children experience recurrent attacks of wheezing and breathlessness (asthma); respiratory infections; chronic inflammation of the nasal passages (atrophic rhinitis); scaling, itchy (pruritic) skin rashes (eczema) etc.[32]

Diagnosis:-
Following diagnostic tools can be useful for further diagnosis.
1. Biopsy of the skin and mucus membranes
2. Sweat pore counts, pilocarpine iontophoresis
3. Genetic testing - genetic mutation analysis may be performed
4. Dental X- ray
5. Dental volumetric CT.

Treatment:-

Medical and Surgical care [1,33]
The care of affected patients depends on which ectodermal structures are involved.

Table – Abnormalities of ED with management

ABNORMALITY	MANAGEMENT AND ADVICE
Anhidrosis/Hypohidrosis	Advice the patient to stay in cool places. Frequent

	consumption of cool liquids
Dental defects	Early dental evaluation and intervention. Complete denture, Removable partial denture, Fixed prosthodontics Over denture or a combination of the above can be selected.
Xerosis or Eczematous dermatitis	Use of topical emollients
Severe alopecia	Advice to wear wigs to improve their appearance. Topical Minoxidil application.
Inflammatory vesicles on scalp	Topical and systemic antibiotics
Reduced lacrimation	Use artificial tears
Nasal mucosal abnormality	Saline sprays followed by the application of petrolatum
Cleft lip or palate and Mid facial defects Hand/foot deformities	Surgical repair

Conclusion:-

In this review the diseases, its causes, symptoms, types & treatment of Ectodermal Dysplasia have been given. It has been seen that, there is no specific treatment for Ectodermal Dysplasia, only disease management is available depending on abnormality. So, we have concluded that further research work has been needed for better understanding of mechanisms involved in the onset and highly effective safe treatment of Ectodermal Dysplasia.

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